

Amendments to the Claims:

This listing of claims replaces all prior versions and listings of claims in the application:

Listing of Claims:

1. (Currently amended) A method of screening for agonistic antibodies that comprises the following steps (a) to (c):

(a) providing a cell that expresses both a multimer-forming receptor and a test antibody, wherein the cell grow depending on the corresponding ligand of the receptor;

(b) determining the test antibody to comprise agonistic activity when autocrine cell growth is autonomous; and

(c) selecting those antibodies as that comprise agonistic activity.

2. (Original) The method of claim 1, that further comprises the step of introducing a gene that encodes the heavy chain of the test antibody₁ into the cell of step (a) having been introduced with a gene that encodes the light chain of the test antibody₁ and a gene that encodes the receptor.

3. (Previously presented) The method of claim 1 wherein the receptor is a chimeric receptor with a protein that comprises a function of transducing a cell growth signal.

4. (Previously presented) The method of claim 1 wherein the receptor is a dimer-forming receptor.
5. (Previously presented) The method of claim 4 wherein the dimer-forming receptor is a homo-dimer.
6. (Previously presented) The method of claim 4 wherein the dimer-forming receptor is a hetero-dimer.
7. (Previously presented) The method of claim 1 wherein the protein that comprises the function of transducing a cell growth signal is a G-CSF receptor.
8. (Previously presented) The method of claim 1 that comprises the introduction of an antibody library to the cell.
9. (Previously presented) The method of claim 8 wherein the antibody library is a retroviral antibody library.
10. (Previously presented) The method of claim 1 wherein the test antibody is a multi-specific antibody.

11. (Original) The method of claim 10 that comprises linking the test antibody's heavy and light chain variable regions with a linker.

12. (Original) The method of claim 11 that comprises producing the antibody with variable regions linked by a linker, using a method that comprises the steps (a) to (c):

(a) producing a single chain Fv against the first receptor chain;

(b) producing a single chain antibody against the first receptor chain by linking the single chain Fv with a CH1-hinge-CH2-CH3; and

(c) producing a multi-specific antibody that comprises the single chain antibody produced in step (b).

13. (Original) The method of claim 11 that comprises producing the antibody with its variable regions linked by a linker, using a method that comprises the steps (a) to (c):

(a) producing a single chain Fab against the first receptor chain;

(b) producing a single chain antibody against the first receptor chain by linking the single chain Fab with an Fc; and

(c) producing a multi-specific antibody that comprises the single chain antibody produced in step (b).

14. (Withdrawn) A method of screening for an agonist multi-specific antibody that comprises the steps (a) to (c):

(a) contacting between a multi-specific antibody and a receptor comprising a first receptor chain and a second receptor chain, where the multi-specific antibody comprises a variable region that can bind with the first receptor chain and a variable region that can bind with the second receptor chain;

(b) determining whether the test multi-specific antibody comprises agonistic activity; and

(c) selecting antibodies that comprise agonistic activity.

15. (Withdrawn) The method of claim 14 that comprises expressing the receptor and the test multi-specific antibody in the same cell.

16. (Withdrawn) The method of claim 15 wherein the cell is a cell that grows depending on the corresponding ligand of the receptor.

17. (Withdrawn) The method of claim 15 wherein the receptor comprises the function of transducing a cell growth signal.

18. (Withdrawn) The method of claim 17 wherein the receptor is a chimeric receptor with a protein that comprises the function of transducing a cell growth signal.

19. (Withdrawn) The method of claim 18 wherein the protein that comprises the function of transducing a cell growth signal is a G-CSF receptor.

20. (Withdrawn) The method of claim 15 wherein the test multi-specific antibody is determined to comprise agonistic activity when autocrine cell growth is autonomous.

21. (Withdrawn) The method of claim 15 that further comprises the step of introducing an antibody library against the first receptor chain and the second receptor chain into the cell, respectively.

22. (Withdrawn) The method of claim 21 wherein the antibody library is a retroviral antibody library.

23. (Withdrawn) The method of claim 14 that comprises linking the light chain variable regions and heavy chain variable regions of the multi-specific antibody with a linker.

24. (Withdrawn) The method of claim 23 that comprises producing a multi-specific antibody with variable regions linked by a linker, using a method that comprises steps (a) to (c):

(a) producing a single chain Fv against the first receptor chain;

(b) producing a single chain antibody against the first receptor chain by linking the single chain Fv with a CH1-hinge-CH2-CH3; and

(c) producing a multi-specific antibody that comprises the single chain antibody produced in step (b).

25. (Withdrawn) The method of claim 23 that comprises producing the multi-specific antibody with variable regions linked by a linker, using a method that comprises steps (a) to (c):

(a) producing a single chain Fab against the first receptor chain;

(b) producing a single chain antibody against the first receptor chain by linking the single chain Fab with an Fc; and

(c) producing a multi-specific antibody that comprises the single chain antibody produced in step (b).

26. (Withdrawn) The method claim 14 that comprises the introduction of “Knobs-into-holes” by amino acid substitution at the CH3 region of the multi-specific antibody.

27. (Withdrawn) The method claim 14 wherein the multimer of the receptor is a heterodimer.

28. (Withdrawn) The method claim 14 wherein the multi-specific antibody is a bispecific antibody.

29. (Withdrawn) A method for producing an agonistic antibody comprising steps (a) to (c):

(a) screening for an agonistic antibody by a method claim 1;

(b) introducing a gene that encodes the agonistic antibody selected by the screening of step (a) into a host cell;

(c) recovering the agonistic antibody from the host cell of step (b) or its cell culture supernatant.

30. (Withdrawn) A cell that expresses an antibody, and a receptor that multimerizes by binding with the antibody, where the cell grow depending on the corresponding ligand of the receptor.

31. (Withdrawn) The cell of claim 30 where the receptor is a chimeric receptor with a protein that comprises the function of transducing a cell growth signal.

32. (Withdrawn) The cell of claim 30 wherein the antibody is a multi-specific antibody.

33. (Withdrawn) The cell of claim 30 wherein the receptor that is multimerized by binding with the antibody comprises the function of transducing a cell growth signal.

34. (Withdrawn) A multi-specific agonistic antibody that comprises the linking of the light chain variable region and heavy chain variable region by linkers, and the introduction of "Knobs-into-holes" by amino acid substitution at the CH3 region of the antibody.